

**REMARKS**

Reconsideration of this application is respectfully requested.

Claims 1-23 and 34 are canceled, and claims 24 and 48 are amended. Those amendments find support at paragraph 036 of the specification, for example, and do not introduce new matter.

The Examiner acknowledged Applicant's claim of foreign priority but requested that Applicant file a certified copy of that priority application. Applicant is obtaining a certified copy of the priority French Application No. 02 11724, filed September 23, 2002, and will file that certified copy as soon as possible.

**Double Patenting**

Claims 1-49 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of Application No. 10/665,872. Application No 10/665,872 has become abandoned and that rejection is therefore moot. Applicant requests that the rejection be withdrawn.

Claims 1-49 also stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-16 of copending Application No. 10/808,410, in view of U.S. Patent No. 5,744,132 and U.S. Patent No. 6,617,316. Applicant requests that the Office hold that rejection in abeyance until one of the allegedly conflicting claims is allowed.

Claims 1-49 also stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-18 of

copending Application No. 10/808,409. Applicant requests that the Office hold that rejection in abeyance until one of the allegedly conflicting claims is allowed.

### **Anticipation**

Claims 1, 2, and 5 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Mourier et. al. (US Patent No. 6,617,316). Claims 1, 2, and 5 are canceled herein. Therefore, that rejection is moot and should be withdrawn.

### **Obviousness**

Claims 3-4 and 6-49 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Mourier (US Patent No. 6,617,316), in view of Debrie (U.S. Patent No. 5,389,618), Lopez (U.S. Patent No. 4,981,955), Sasisekharan (U.S. Patent No. 5,569,600), Petitou (U.S. Patent No. 4,801,583) and Bergendal (U.S. Patent No. 5,039,529).

According to the Examiner Mourier teaches a method for analyzing heparins comprising depolymerizing a sample with heparinases, and assaying by HPLC, at column 2, lines 30-35 and line 48, and at column 3, line 13 and lines 27-28. The Examiner states that the oligosaccharides present are modified with a 1,6-anhydro bond and the chromatography is anion exchange.

The Examiner cites Debrie as teaching enoxaparin and a mobile phase chromatography region up to 206 nm wherein phosphate salt buffer is used, Lopez as teaching a reducing agent for depolymerized heparin, i.e. sodium borohydride (alkali metal salt of borohydride), Sasisekharan as teaching a mixture of heparinases,

including I, II and III, Petitou as teaching an oligosaccharide comprising at least one 1,6-anhydro residue, and Bergendal as teaching acetylated sugars and detection of components.

The Examiner acknowledges that the claims differ from the teachings of Mourier "in that a mixture of enzymes, reducing agent: borohydride, enoxaparin, mobile phase and acetylated sugars are not specifically disclosed." However, according to the Examiner:

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of Mourier et al, Debrie, Lopez, Sasisekharan et al, Petitou et al and Bergendal et al in order to provide for an analyzing method for enoxaparin selecting a mixture of heparinases of I, II, III, for which to depolymerize and then reduce the depolymerizant with borohydride for detection of components such as acetylated sugars as all of these claimed features are disclosed by the secondary cited references. One of skill would have expected successful results for depolymerizing enoxaparin and to then reduce it by the disclosed agent is clearly taught. Further, to detect other components, such as acetylated sugars, upon applying mobile phase and HPLC chromatography for analyzing a sample containing heparin is clearly within the skill of an artisan. Further, to modify the oligosaccharides with 1,6-anhydro bond is clearly an obvious modification as it clearly prevalent and disclosed by Peitou et al to be an obvious and desirable bond for which to modify oligosaccharide components from a depolymerized sample as disclosed by Mourier et al. One of skill would have been motivated to perform the steps as claimed because they are clearly disclosed in the cited prior art for analyzing a heparin containing sample. Furthermore, depolymerization with a mixture of heparinases is clearly disclosed as well. In the absence of unexpected successful results the claims are rendered *prima facie* obvious over the cited prior art.

Applicant respectfully traverses the rejection. During Examination "The examiner bears the initial burden of factually supporting any *prima facie* conclusion of

obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness." M.P.E.P. § 2142. "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." M.P.E.P. § 2142. Applicant will show that the Office has not met *any* of the required elements to make out a case of *prima facie* obviousness.

Amended claim 24 recites "[a] method for detecting and quantifying the components in a sample of material chosen from unfractionated heparins and fractionated heparins." That method comprises three recited elements:

- (a) exhaustively depolymerizing said sample by an enzymatic method;
- (b) reducing the depolymerized sample of step (a); and
- (c) detecting and quantifying the components in the reduced sample of (b) by high-performance liquid chromatography.

The claim further recites that the HPLC is performed "in a mobile phase which is transparent to UV light with wavelengths from about 200 nm to about 400 nm, wherein the mobile phase does not comprise NaCl." The method results in "detect[ing] and quantify[ing] the components in the sample."

That method is not disclosed in Mourier as the Examiner admits. The methods of Mourier do not combine “exhaustively depolymerizing” the sample, “reducing the depolymerized sample,” and HPLC “in a mobile phase which is transparent to UV light with wavelengths from about 200 nm to about 400 nm, wherein the mobile phase does not comprise NaCl.” Further, the methods Mourier discloses are aimed at characterizing a sample that is not exhaustively depolymerized. Accordingly, Mourier’s disclosed methods do not “detect and quantify the components in the sample,” as in the claims.

Nothing in the other references cited remedies the deficiencies of Mourier. For example, nothing in the references suggests exclusion of NaCl from the HPLC mobile phase, as in the claims. The references also do not suggest how to arrive at a method that provides “detect[ing] and quantify[ing] the components in the [starting] sample,” as in the claims.

For the foregoing reasons the claims are nonobvious over the cited art and this rejection should be withdrawn.

## Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge  
any additional required fees to our Deposit Account 06-0916.

Respectfully submitted,

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